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FORM PTO-1390 (REV. 12-2001) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER	U.S. APPLICATION NO. (If known, see 37 CFR 1.5
S04P03US	10/070347

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/DE00/02930	8/28/2000	8/28/1999

TITLE OF INVENTION: Computer-Based Method for Automatically Processing Data, Especially Magnetocardiographic Data, of Biomagnetic Fields

APPLICANT(S) FOR DO/EO/US: Stella Romanovych for Stepanowitsch Romanovych (deceased) and Fritz Steinberg

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [X] This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. [X] The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is attached hereto (required only if not communicated by the International Bureau).
   b. [X] has been communicated by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [X] An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. [X] is attached hereto.
   b. [ ] has been previously submitted under 35 U.S.C. 154(d)(4).
7. [ ] Amendments to the claims of the International Aplication under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are attached hereto (required only if not communicated by the International Bureau).
   b. [ ] have been communicated by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
8. [ ] An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. [ ] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. [ ] An English lanugage translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [X] A FIRST preliminary amendment.
14. [ ] A SECOND or SUBSEQUENT preliminary amendment.
15. [ ] A substitute specification.
16. [ ] A change of power of attorney and/or address letter.
17. [ ] A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
18. [ ] A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. [ ] A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. [X] Other items or information: Application Data Sheet

"Express Mail" Label # EU 091 927 914 US - I hereby certify that this paper or fee is being deposited with the USPS "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on **2/28/2002,** and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Gudrun E. Huckett

Gudrun E. Huckett, Patent Agent

U.S. APPLICATION NO. (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
10/070347	PCT/DE00/02930	S04P03US

21. [X] The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):	CALCULATIONS PTO USE ONLY
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$1040.00**	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$890.00**	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$740.00**	
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$710.00**	
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) **$100.00**	
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 890.00
Surcharge of **$130.00** for furnishing the oath or declaration later than [ ] 20 [X] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$ 130.00

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	11 - 20 =	0	x **$18.00**	$
Independent claims	1 - 3 =	0	x **$84.00**	$
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ **$280.00**	$

TOTAL OF ABOVE CALCULATIONS =	$ 1020.00
[X] Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2. +	$ 510.00
SUBTOTAL =	$ 510.00
Processing fee of **$130.00** for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)).	$
TOTAL NATIONAL FEE =	$ 510.00
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +	$
TOTAL FEES ENCLOSED =	$ 510.00
Amount to be refunded:	$
charged:	$

a. [ ] A check in the amount of $ _____ to cover the above fees is enclosed.

b. [X] Please charge my Deposit Account No. 50-1199 in the amount of $ 510.00 to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [X] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-1199. A duplicate copy of this sheet is enclosed.

d. [ ] Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Gudrun E. Huckett, Patent Agent
P.O. Box 3187
Albuquerque, NM 87190-3187

Gudrun E. Huckett
SIGNATURE
Gudrun E. Huckett
NAME
35,747
REGISTRATION NUMBER
2/28/2002

S04P03US

APPLICATION DATA SHEET

INVENTOR INFORMATION

Inventor One Given Name:	Stepanowitsch
Family Name:	Romanovych (deceased)
Citizenship:	Ukraine
Inventor Two Given Name:	Fritz
Family Name:	Steinberg
Postal Address Line One:	Mausegattstr. 29
City:	Mülheim an der Ruhr
Postal or Zip Code:	45472
Country:	Germany
Citizenship:	Germany

APPLICANT INFORMATION - Applicant for Inventor One

Given Name:	Stella
Family Name:	Romanovych
Authority:	heiress to Stepanowitsch Romanovych
Postal Address Line One:	c/o Squid AG
Postal Address Line Two:	Kruppstrasse 94
City:	Essen
Postal or Zip Code:	45145
Country:	Germany

CUSTOMER NUMBER

30008
PATENT & TRADEMARK OFFICE

CORRESPONDENCE INFORMATION

Name Line One:	Gudrun E. Huckett, Ph.D.
Address Line One:	P.O. Box 3187
City:	Albuquerque
State or Province:	NM
Postal or Zip Code:	87190-3187

S04P03US

Telephone One:	(505) 266-2138
Telephone Two:	(505) 268-7798
Fax:	(505) 266-2138
Electronic Mail:	gehuckett@uswest.net

REPRESENTATIVE INFORMATION

Registration Number:	35,747

APPLICATION INFORMATION

Title Line One:	Computer-Based Method for Automatically
Title Line Two:	Processing Data, Especially Magneto-
Title Line Three:	cardiographic Data, of Biomagnetic Fields
Total Drawing Sheets:	1
Formal Drawings:	Yes
Application Type:	Utility
Docket Number:	S04P03US

ASSIGNEE INFORMATION

Company Name:	Squid AG
City:	Essen
Country:	Germany

PRIOR FOREIGN APPLICATIONS

Foreign Application One:	19940912.9
Filing Date:	8/28/1999
Country:	Germany
Priority Claimed:	YES
Foreign Application Two:	PCT/DE00/02930
Filing Date:	8/28/2000
Country:	WIPO

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Date of Deposit February 28, 2002
I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Gudrun E. Huckett
Gudrun E. Huckett, Patent Agent

Applicant:	Stepanowitsch Romanovych, et al.
Serial No:	not yet known (based on PCT/DE00/02930)
International Filing Date:	8/28/2000
U.S. Filed:	2/28/2002
Title:	Computer-Based Method for Automatically Processing Data, Especially Magnetocardiographic Data, of Biomagnetic Fields

Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to the first office action, please amend the instant application as follows:

IN THE CLAIMS:

Cancel claims 1-14.

Please add new claims 15-25.

IN THE ABSTRACT:

Please add the attached Abstract of the Disclosure to the specification.

REMARKS

Claims 1-14 have been cancelled and replaced with claims 15-25 drafted in proper U.S. format. A proper Abstract of the Disclosure has been added to the specification.

In view of the foregoing, it is submitted that this application is now in condition for allowance and such allowance is respectfully solicited.

Authorization is herewith given to charge any fees or any shortages in any fees required during prosecution of this application and not paid by other means to Patent and Trademark Office deposit account 50-1199.

Respectfully submitted on February 28, 2002,

Gudrun E. Huckett

Gudrun E. Huckett, Ph.D.
Registration No. 35,747

Gudrun E. Huckett, Patent Agent
P.O. Box. 3187
Albuquerque, NM 87190-3187

Telephone: (505) 266-2138
Facsimile: (505) 266-2138

GEH/Encl.: new claims 15-25; Abstract

NEW CLAIMS 15-25

15. A computer-based method for automatically processing magnetocardiographic data of biomagnetic fields, based on a surface density of magnetic moments (layer of magnetic dipoles) or a function of currents as physical and mathematical models of sources of the biomagnetic field, the method comprising the steps of:

stating an integral equation of the surface density of the magnetic moments, wherein a right term of the equation represents a second differentiation of the magnetic field induction measured by a gradiometer in the normal direction to the measuring plane ($\partial^2 B_z/\partial z^2$);

determining analytical expressions for factors of a matrix A which approximates the integral operator of the integral equation and computing this matrix;

interpolating the measured values of the function $y=\partial^2 B_z/\partial z^2$ in the nodes of a preferably small-dimensioned grid;

solving according to Tickhonov a linear algebraic equation system Ax=y, wherein x is the surface density of the magnetic moments;

constructing contour line maps of the surface density of the magnetic moments or a current line map, equivalent to the contour line maps, and reading the map into a storage unit or an output unit.

16. A method according to claim 15, wherein the gradient of the surface density of the magnetic moments is automatically calculated and the map of the current density is constructed and is read into a storage unit or an output unit.

17. A method according to claim 15, wherein at least selected data are compared according to predetermined criteria automatically with at least one predefined

normal value and that, upon deviation of the data from the normal value by a predetermined amount, a signal is generated which can be output on an output device and which signals the deviation.

18. A method according to claim 17, wherein the magnitude of the fields under the P-wave and the QRS complex are calculated, wherein the magnitude of the fields reflects the energy generated during the excitation of the atria and ventricles of the heart, wherein a ratio of these fields is calculated in order to estimate the electrical activity of the atria in comparison to the electrical activity of the ventricles in order determine parameters related to the degree of heart failure.

19. A method according to claim 15, wherein the measured data are subjected automatically pass to different analysis steps and wherein the complexity of the analysis increases with each analysis step.

20. A method according to claim 19, wherein at least one of the following analysis steps is employed:

amplitude-time analysis of different MCG curves;

analysis of high-resolution MCG;

analysis of the sum of MCG and vector MCG (VMCG);

qualitative analysis of the magnetic field distribution maps;

quantitative analysis of the magnetic field distribution maps;

analysis of the effective dipole characteristics;

analysis of two-dimensional charge distribution; and

analysis of three-dimensional charge distribution.

21. A method according to claim 15, further comprising the steps of:

estimating the alternating arrangement of maximum positive and negative extreme values in each magnetic field distribution map;

estimating the direction of equivalent current dipoles in each map by using the right-hand rule;

estimating the presence of additional extreme values in each magnetic field distribution map and duration of their existence during the repolarization process;

calculating the ratio of the maximum negative to the maximum positive extremes in each map and of the standard differentiation of these parameters during the method;

estimating the effective dipole depth curve in the repolarization;

estimating the distribution and alternating arrangement of current line and the directions of current line vectors in each map during the repolarization;

estimating the curves of average and maximum current density during repolarization;

automatically evaluating ventricular repolarization with respect to conformity of the actual repolarization process in comparison to normal parameters.

22. A method according to claim 15, further comprising the steps of:

estimating the alternating arrangement of maximum positive and negative extreme values in each magnetic field distribution map;

according to the right-hand rule, estimating the direction of the equivalent current dipole in each map;

estimating the presence of additional extreme values in each magnetic field distribution map and the duration of their presence during the depolarization process;

estimating the effective dipole depth curve during the depolarization;

estimating the distribution and alternating arrangement of current lines and the directions of the current density vectors in each map during the depolarization;

estimating the duration of existence of additional current areas during the depolarization process;

estimating the curve of average and maximum current density during the depolarization;

automatically evaluating conformity of the actual the depolarization process with normal parameters.

23. A method according to claim 15, further comprising the steps of:

estimating the alternating arrangement of maximum positive and negative extreme values in each magnetic field distribution map;

estimating according to the right-hand rule the direction of equivalent current dipoles in each map;

estimating the presence of additional extreme values in each magnetic field distribution map and the duration of their existence during the repolarization process;

determining the ordinal number of the map beginning at the point in time at which the direction of the equivalent current dipole of the ventricular repolarization became stably normal (oriented to the left and downward);

estimating the effective dipole depth at the J point;

estimating the distribution and alternating arrangement of the current lines and the directions of current density vectors in each map during the repolarization;

determining the ordinal number of the map beginning at the point in time at which the direction of maximum current density vector of the ventricular repolarization became stably normal, i.e., oriented to the left and downward;

estimating the duration of existence of additional current areas during repolarization process;

estimating the curves of average and maximum current density during the repolarization at the beginning of the ST-T interval;

estimating the ratios of maximum and average current densities in the QRS maximum relative to those at T-maximum;

automatically evaluating the estimations with respect to the presence and severity of myocardial ischemia.

24. A method according to claim 15, further comprising the steps of:

estimating the alternating arrangement of maximum positive and negative extreme values in each magnetic field distribution map;

estimating according to the right-hand rule the direction of the equivalent current dipoles in each map;

determining the time periods during which the direction of the effective dipoles remains oriented 1. to the right or to the right and downward, 2. to the left and downward, 3. to the right or to the right and upward;

estimating the presence of additional extreme values in each magnetic field distribution map and the duration of their existence during the depolarization process;

estimating the relative amplitude of the upwardly and downwardly oriented movement of the effective dipoles during the depolarization;

estimating the distribution and alternating arrangement of a current line and the directions of current density vectors in each map during the depolarization;

determining the time period during which the direction of maximum current density vectors remains oriented 1. to the right or to the right and downward, 2. to the left and downward, 3. to the right or to the right and upward;

estimating the duration of existence of additional current areas during the

depolarization process;

estimating the peak values of the average and maximum current density during the depolarization and the form of the corresponding curves;

automatically evaluating the estimations with respect to the presence of myocardial necrosis.

25. A method according to claim 15, wherein upon comparison of the considered data with normal values, the considered data are automatically stored in a self-learning database and, according to predetermined criteria, are employed for a continuous formation and checking of normal values and tolerable deviations of the normal values.

Abstract of the Disclosure

In a computer-based method of processing magnetocardiographic data of biomagnetic fields for making the currents causing the biomagnetic field visible to a physician for diagnostic purposes, an integral equation of the surface density of the magnetic moments is provided, wherein the right part of the equation represents a second differentiation of the magnetic field induction measured by a gradiometer in the normal direction to the measuring plane. Analytical expressions for factors of a matrix A are determined which approximates the integral operator and the matrix is computed. The measured values of the function $y=\partial^2 B_z/\partial z^2$ in the nodes of a grid are interpolated and a linear algebraic equation system $Ax=y$, wherein x is the surface density of the magnetic moments, is solved according to Tickhonov. Contour line maps of the surface density of the magnetic moments or current line maps are constructed and stored or displayed.

Computer-Based Method for Automatically Processing Data, Especially Magnetocardiographic Data, of Biomagnetic Fields

The invention relates to a computer-based method for automatically processing data of biomagnetic fields, in particular, of magnetocardiographic data. In particular, the invention relates to a method that makes it possible to automatically visualize biomagnetic fields, measured within one plane or at several points of the plane by means of one or several detectors, in particular, by means of a SQUID detector, for example, in the form of magnetic field maps and to automatically evaluate and classify the information contained in the field.

Since biomagnetic fields - in contrast to electrical fields - do not expand by means of conductors and are substantially measurable in an unaltered way outside of a biological body, for example, in a plane across the human heart in a non-invasive way, the measurement of biomagnetic fields by means of new, highly sensitive detection devices, such as, for example, a magnetograph described in the international patent application PCT/DE00/02472, which can be used advantageously in an unshielded environment, represents a technology which will find broad medical application in the coming years. In particular, preventive examinations are possible in which large groups of the population can be examined with regard to heart attack risk in a simple and fast way.

The development of highly sensitive magnetographs, in particular, such devices which can be used in unshielded environments, requires new methods for processing the measured data since the current known methods are extremely time-consuming and can be performed only by a few specialists. The data are to be processed substantially automatically such that the diagnostically relevant information contained in the measured magnetic fields can be easily recognized ad evaluated by a physician. In a preferred embodiment, the method is to be designed to compare and automatically classify the diagnostically relevant information

contained in the data with stored information in order to thus assist the physician in his diagnosis. Certain information is to be visualized, for example, in the form of current line maps.

When it is desired to represent biomagnetic currents, in particular, the currents within the heart, which in clinical diagnostics have proven to be of specially high relevance, a so-called "inverse problem" must be solved, i.e., based on the detected magnetic fields, which are caused by the biomagnetic currents, the currents causing the fields are to be calculated.

In view of the complexity of inverse problems for the localization of magnetic field sources, different simplifying assumption are made for solving the problem. One of these assumptions is, for example, that all sources are positioned in the same plane and are arranged at a certain distance from a measuring surface. The obtained results depend on which physical model and, correspondingly, which mathematical model is selected as a model for the magnetic field sources. In the case that a flat source area is selected, conventionally the distribution of the current densities on the surface is selected as a model of the sources which represents the detected vector magnitude. After solving an inverse problem, a map of directional arrows is obtained whose magnitude is proportional to the amount of current density.

The representation of currents in such a way results in certain difficulties. With respect to the calculated area where the modulo value of the current densities is several times smaller than the maximum, it is not easily possible to estimate the magnitude and direction of the arrows based on the map of arrows. The sources with smaller intensity thus are dropped from the examination.

A method for automated visualization of the heart currents by current lines in the plane is described in the article by R. Killman, G.G. Jaros, P. Wach, R. Graumann, W. Moshage, M. Renhard, P.H. Fleischmann: Localization of Myocardial Ischemia from the Magnetocardiogramm Using Current Density Reconstruction

Method: Computer Simulation Study, Biological Engineering & Computing, September 1995, pp. 643-651. According to the method described in the aforementioned article, the result of solving the inverse problem is one of the aforementioned maps with oriented arrows whose magnitude is proportional to the modulus of the current density.

The method known from the aforementioned article for representing heart currents by current lines in the plane has, however, the disadvantages that in the areas in which the current density modulo 3 and more is smaller than the maximum, a visual evaluation of the pattern of arrows generated with the method with regard to their magnitude and direction is no longer easily possible. In practice, it was found that with respect to a reasonable error estimation only one to two specially intensive areas of the magnetic field can be visualized. The other, less intensive areas cannot be identified visually.

Based on this, the invention has, on the one hand, the object to provide a method for processing the data of a detected biomagnetic field by which the currents causing the biomagnetic field can be visualized by current lines in the plane and thus are made accessible for a visual evaluation by trained personnel or a physician in an especially simple way.

The object is solved by a method with the features of claim 1.

As a model of the biological currents according to the invention the surface density of a double layer of magnetic charges (simple layer of magnetic dipoles) or, which is equivalent to this, a function of the currents is selected. An important property of this function is that the projection of its contour lines onto a calculated plane represent current lines. Accordingly, one obtains, by solving an integral equation concerning the density of a double layer of magnetic charges, a map of current lines wherein the terms to the right of the equation represent the distribution of the magnetic field (components of the magnetic induction vector or its differentiations), for example, measured in a plane near the thorax.

According to the invention it is assumed that the actually voluminous sources of the field are arranged in a (calculated) plane which extends parallel to the measured plane. According to an acceptable physical and mathematical model of the sources of a magnetic field, an integral equation is stated and solved whose right term represents the measured magnetic fields and whose solution is the distribution of its sources in the examined body, i.e., for example, in the heart. Should these sources have the character of separate magnetic dipoles whose axes extend perpendicularly to a plane, they are interpreted as magnetic sheets and, when viewed as a map, preferably colored, that is output by employing the method on an output unit, for example, a monitor or a printer, they look like separate current vortices.

The important novelty resides in the treatment of the physical and mathematical model of the sources of an elementary magnetic field in a plane as function of the current and its use in an integral equation as the desired unknown parameter. The contour lines of the equation which are obtained after solving this equation (lines of constant values) represent the current lines.

The maps of the current lines, in comparison to the maps of the current density vectors (arrows), provide a better visual representation of the expansion of a current in a calculated plane. On a map of current lines the sources of large as well as small intensities are precisely represented. The current vortices which are near the calculated area locations are represented independent of their magnitude and intensity. Accordingly, the method makes it possible to view not only conventional patterns of biological currents of, for example, the heart, but also to differentiate details of this current flow.

The results of solving the inverse problem by the aforementioned method makes it possible to construct maps of current density vectors; in contrast, the results, which are obtained with the prior art methods, cannot be used for the purpose of producing current line maps.

The current function is a scalar expression and the current density is a vector which has two projections in the plane. Accordingly, for the same plane network the amount of required values of a current function is two times smaller than the amount of the required values when considering the projections of current density vectors. Accordingly, the order of the linear algebraic equation system to be solved is two times lower.

After solving the algebraic system and differentiation of a current function it is possible to determine the distribution of the current density vectors as in the traditional formulation.

The illustration of the currents in the plane by current lines makes it possible to substantially improve the precision of the solution so that it is possible to visualize even smaller details including the current vortices of a small diameter.

When the measured data are magnetocardiographic (MCG) data, electrical events in the heart are to be evaluated and conclusions in regard to the physiological state of the heart are to be drawn. The information required for this purpose are contained in the magnetic field of the heart recorded above the thorax surface but, as a result, of their "cryptic" form are not suitable for a direct interpretation. A special object of the invention is therefore the processing of such magnetocardiographic data which change during the cardial cycle such that a physician can obtain directly information in regard to the physiological state of the examined heart. For this purpose, a durable and clear system of diagnostic criteria should be developed, comparable to the standard criteria sets known from electrocardiology (ECG).

For this purpose, a computer-based method for automatically processing data of biomagnetic fields, in particular, of magnetocardiographic data, is suggested in which at least selected data are automatically compared according to preset criteria with at least one predefined normal value and, in the case of deviation of the data from the normal value by a predetermined amount, a signal is generated

that can be output on an output unit and indicates the deviation. The signal can be output in the form of an acoustic, in particular, however, an optical signal, for example, by representing the value determined based on the data in red, while normal values are represented in black or green.

According to the invention, the measured data pass for this purpose automatically through different analytical steps wherein the complexity of the analysis increases with each step. The individual steps are compiled in Table 1. In detail, the following analysis steps are performed:

1. Amplitude-time-analysis of different MCG curves.
2. Analysis of high-resolution MCG.
3. Analysis of the sum of MCG and vector MCG (VMCG).
4. Qualitative analysis of the magnetic field distribution maps.
5. Quantitative analysis of the magnetic field distribution maps.
6. Analysis of the effective dipole characteristics.
7. Analysis of the two-dimensional charge distribution.
8. Analysis of the three-dimensional charge distribution.

The first analysis step is similar to the method for the morphological analysis of conventional ECG, in particular, since MCG curves look similar to ECG curves, and both have the same nomenclature of waves and intervals - PQRST. In this analysis step it is already possible to detect myocardial ischemia.

In the second analysis step, the spectral-temporal analysis (i.e., the determination of the relative energy of a cardial signal spectrum for different frequency bands and determination of spectral variability) and time range analysis (primarily of QRS duration) of the signal), an average of the MCG is formed at different measured points. Conventionally, the purpose of such an analysis is the determination of the homogeneity of the ventricular depolarization and use of these data for the evaluation of the risk of occurrence of arrhythmia. Such an approach is also used in order to estimate the risk of rejection of transplants.

In the third analysis step the sum of all measured points is created. Such an approach provides a more generalized representation in regard to some properties of the myocardial excitation. It is especially advantageous to calculate the fields under the P-wave and the QRS complex. The magnitude of these fields represents the energy which is generated curing excitation of the atria and ventricles of the heart. Moreover, the ratio of these fields can be calculated in order to estimate in this way the electrical activity of the atria in comparison to electrical activity of the ventricles. It has been found that this parameter is related to the degree of heart failure.

In this same analysis step the data of a vector MCG can also be employed which are registered in special single-positional Leads systems. The amplitude values of the X, Y, and Z components during the P-wave, the QRS complex, and the ST-T interval, the amplitude and direction of the spatial maximum QRS vector, the QRS vector duration etc. can be calculated and employed for the diagnosis of myocardial ischemia. Conventionally, the analyses are carried out together with an ECG analysis.

The information value of the MCG data increases dramatically with the transition to the following step of the analysis, in particular, to the cartographic procedure of the magnetic field (MF mapping). This method means the construction of distribution maps of the induction of the magnetic field in measured points at certain moments within the cardial cycle. These maps are constructed according to the principle of geographic maps, i.e., areas with identical values of certain parameters have the same color. It is important to understand that each map results from all measured points.

The interpretation of electrical activity of the heart based on this approach has a number of essential advantages. Firstly, by means of the interpretation method all important data, including the data which can be obtained between the points of the measuring grid, can be incorporated into the computation. Secondly,

the maps represent a natural projection of the electromagnetic phenomena which have been registered above the thorax surface at different locations of the heart, even if only approximately.

Advantageously, two especially important properties of each magnetic field distribution map can be automatically determined: firstly, the number of extreme values of the magnetic field (in the physical sense, local extreme values of a magnetic field are points with maximum values in comparison to neighboring points), in other words, the inhomogeneity of the map, and, secondly, the alternating arrangement of the extreme values.

The homogeneity of a magnetic field map reflects the homogeneity of the electrical source which induces this map. This, in turn, shows that there are no myocardial locations which differ significantly from neighboring zones with respect to their electro-physiological properties so that there are no local disturbance currents. Normally, the map at any time of the cardial cycle has a dipole structure, i.e., there is only one minimum and one maximum. It is clear that the occurrence of additional extreme values proves the presence of additional local currents.

With respect to physiological considerations, a further important characteristic of the maps, as mentioned above, is the alternating arrangement of minima and maxima of the magnetic field. When a line is from one minimum to a maximum and then, in turn, this line is rotated in a counter-clockwise direction by 90°, the direction obtained will correspond to the orientation of the corresponding charge dipole. This orientation reflects the direction of expansion of the excitation front in the respectively observed moment of the cardial cycle.

Based on this principle, the maps of certain characteristic points in time of the cardial cycle, for example, of the QRS onset, R max, QRS offset, T max, T offset, are visually analyzed. Integrated maps which have been computed during the entire QRS complex and/or the St-T interval, can be examined. The qualitative visual analysis methods for magnetic field maps are sufficient in order to obtain a

general illustration of important properties of the electro-physical process in the myocardium in any individual situation, but they are not able to provide a quantitative description of the detected properties and do not allow to obtain statistical parameters for a group of patients. Therefore, the following step of the analysis of magnetic field distribution maps is the application of the quantitative criteria.

Different quantitative criteria for a versatile evaluation of different maps and time series of maps have been developed.

The simplest approach is the calculation of the number of extreme values in each map and an expansion onto all examined intervals of cardial cycles. In this connection, the relative "smoothness index" is also used which represents the sum of the correlation factors between four sequential maps at the beginning of the ST segment.

In addition, the criterion based on the estimation of the complexity of the trajectories of the extreme values during the ventricular excitation is known also. As a further quantitative criterion the variability of the ratio of the greatest positive and the greatest negative extreme values during the ST-T interval can be used. Moreover, a homogeneity coefficient is known which for integral estimation to estimate the number of extreme values and their sharpness over the ST-T interval. An interesting approach resides in a special spatial transformation (KLM transformation) of the magnetic fields distribution maps and the calculation of the non-dipolar contributions in each map. Sometimes, other quantitative parameters are also used. In addition, some other approaches of magnetic cartography are described in different articles. For example, in an article maps were used, simultaneously with the traditional maps of a magnetic field distribution, which maps represent a spatial distribution of a quantitative index which represents the breakdown of a QRS complex at every point of a measuring grid. This increases the precision of examination for patients with VT. The spatial distribution of the QT

interval and the duration of its parts in combination with the calculation of some smoothness indices is described in another article. The purpose of all these different indices is the same, i.e., providing a quantitative estimation of the degree of inhomogeneity of the magnetic field distribution maps and thus - to a certain degree - of the wave which has produced this field.

In this connection, it is necessary in any case to understand that the estimation of the electrical phenomena in the myocardium on the basis of magnetic field distribution is not a direct estimation.

A more direct and physiologically more valuable information can be derived from the MCG analysis on the basis of solving the inverse electrodynamic problem. Solving the inverse electrodynamic problem in regard to cardiology means the reconstruction of the electrical events in the heart based on the measurements carried out at the surface of a human body. In the case of MCG, the measurement is not carried out on the surface of a body but above the surface in a measuring plane.

It is in principle impossible to calculate the properties of electrical sources in the heart, which generate the ECG, based only on this ECG. As has been mentioned already, the conductivity of tissues and the shape of a body have a substantially smaller effect on the MCG (compared to the ECG) so that the spatial resolution of MCG is substantially greater than that of ECG. Accordingly, a magnetocardiogram allows a substantially more precise solving of the inverse problem, even though sources reconstructed on the basis of an MCG are definitely idealized and do not completely coincide with the actual ones.

There are at least three planes of reconstruction and representation of bioelectrical sources in the heart.

The first plane is a representation of a source as an equivalent dipole. In this connection, it is assumed that the entire electrical activity of the heart is focused in one point. Such a representation does not mean that the heart is actually a point

source. It means that the results of its activity on the surface of a body are equivalent to the effects which can be measured if a point source were present. Such a representation of the source serves as a detection basis of a vector cardiography. It is clear that it does not allow to determine the own activities of different parts of the heart.

The second plane of the data representation on the basis of solving the inverse problem is the reconstruction of the sources in the form of charge distributions in a layer. In this connection two approaches can be used. The first approach resides in the interpretation of the magnetic field source as a map of distribution of charge density vectors, the second approach makes it possible to plot a map of fixed charge lines and is more promising. The image of the charge distribution makes possible already the simultaneous estimation of characteristics of different sources and the excitation of different parts of the heart.

Finally, the third plane resides in the reconstruction of the spatial three-dimensional bioelectrical source, i.e., the reconstitution of sources closest to reality. It is however clear that the reconstruction of three-dimensional sources requires the application off highly complex physical models and mathematical algorithms.

The determination of the position of a point source at the moment of the beginning of an ectopic QRS complex is employed in order to determine the point of origin of ventricular arrhythmia, and the same method is used in the delta wave for additional localization of the path. The strength of the effective dipole in the R maximum point has also been used as a criterion for estimation of the risk of rejection after heart transplants.

Other parameters of the effective dipole - its orientation in a frontal plane in characteristic moments of the cardial cycle - are used as criteria for patients in ischemia diagnosis. In our view, very important information can be derived from the estimation of the dipole behavior not only in certain characteristic moments of the cardial cycle but during the entire excitation process. For example, the shape of the

curves of the dipole orientation and the strength during the QR interval are a sensitive marker for MI. In our articles we analyze the curves of the equivalent dipole depths during the ventricular excitation, i.e., the character of the dipole movement in its forward-backward direction. We suppose that to a certain degree the curve represents the distribution of the sources in a sagittal plane, which conventionally is outside of the analysis because MCG conventionally is registered only in a frontal plane. Therefore, it is possible to view the common analysis of field (or charge) distribution maps and the curve of one source depth as a simplified analysis of a three-dimensional charge distribution. As expected, the analysis appears to be very informative for the diagnosis of MI including non-Q MI.

The analysis of the distribution maps of the charge density vectors or charge lines provides additional options in comparison to the preceding analysis planes. It is important to note that these levels of analysis are characteristic only for MCG and, as far as we know, have no analogy in the ECG diagnosis. It enables visualization of an image of the charge distributions in the myocardium including the so-called "disturbance currents".

The presence and direction of these currents is estimated visually. As a quantitative estimation of the current distribution, the current density value is employed, for example, at the peak of the QRS complex. We analyze the curve of the maximum and the average current density in each map during the entire cardial cycle. Such an analysis appears to be very useful for the different types of ischemia.

According to the invention, moreover, an automated method is suggested which provides the physician with the possibility of estimating the number, direction, intensity, and magnitude of current vortices at any moment of the cardial cycle and thus their behavior during the depolarization or repolarization.

It is expedient, parallel to the magnetocardiography it is necessary, to employ a heart visualization method, such as, for example, x-ray, computer tomography,

nuclear magnetic resonance tomography etc. Which one of these methods should be selected, depends on the requirements in regard to a detailed resolution of the anatomic information which, in turn, depends on the concrete clinical objective. Practical experience has shown that in most cases it is sufficient to employ simple x-ray or that it is even possible to employ no heart visualization method at all without this causing a reduction of the value of the MCG examination.

In the analysis according to Table 1, each sequential step of the analysis is specified and develops further information which has been obtained in the preceding stage. For example, the sensitivity of the algorithm in the diagnosis of IHD , when only the analysis of the magnetic field distribution maps would be used, would only be 86 %. If in addition thereto the analysis based on solving of the inverse problem was employed, the sensitivity was increased to 94 %.

The form of the medical conclusion which is made by the magnetocardiographologist and is submitted to the clinician, is very important. Conclusions are employed which are comprised of two parts. In the first part the quantitative and semi-quantitative characteristics of the actual MCG are provided (homogeneity of the maps, orientation of the ECD, and of the vectors of the current density, current density values etc.).

In the second part of the conclusion, the discovered changes are automatically brought in correlation with physiological conclusions or types of heart diseases, for example: "... disruptions which were during the ventricular repolarization, relate to high (average, minimal) probability of IHD" or "... of a high risk of occurrence of arrhythmia" or "in comparison with preceding MCG significant positive change are exhibited which confirm the efficiency of an anti-angina (anti-arrhythmic) therapy".

Of course, the suggested interpretation schematic and the form of the conclusions are not complete and are not the only ones possible. Each interpretation level and the separate parameters require a detailed analysis based

on the information theory. Overall, it is possible to provide a set of formalized decision rules for the diagnosis of different heart states based on the MCG data.

Without doubt, the development and standardization of a schematic for the medical interpretation of MCG is one of the most important necessary requirements for a broad application of the method.

In any case, it is already possible to recognize that the provided criteria and the interpretation schematic make the use of MCG as a real and actually useful diagnostic tool to be recognized.

In general, all criteria can be divided into four groups. Within the groups they are arranged in ascending sequence of the analysis steps.

Group 1. Criteria for estimation of signal-noise ratio.

A. Visual estimation of high-frequency-low-amplitude waves along with the average MCG curves.

Group 2. Criteria for the estimation of excitation homogeneity.

A. Visual estimation of the difference of the magnetic field maps.

B. Quantitative analysis of the number of extreme values. In this connection, the normal value is not more than three extreme values in each map.

C. Coefficient of homogeneity (CH). The normal value is not more than 0.95.

D*. $\delta_{min/max}$ during the ST-T interval (min/max ratio of the maximum negative extreme values to the minimal negative extreme values at each point in time). The normal value is not greater than 0.15.

E*. δZ_0 during the ST-T interval (Z_0 - depth of the effective dipole at each point in time). The normal value is not more than 0.20.

F. Visual estimation of the difference of the current distribution maps.

G*. Quantitative analysis of the current vortex number. The normal value is not more than three vortices in each map.

The main clinical significance of the group of criteria is the determination of heart disturbances in general and, in particular, the determination of risk of cardial

arrhythmia and the estimation of the effectiveness of an anti-arrhythmic therapy.

Group 3. Criteria for the analysis of excitation of the direction of the wave distribution.

A. Visual estimation of the approximate direction of the corresponding current dipole based on the magnetic field distribution maps.

B*. Quantitative analysis of the corresponding current dipole orientation based on the magnetic field distribution maps. The normal orientation during the ST-T interval is to the left and downward (during not more than 2/3 of the duration of the ST-T interval). The normal orientation during the QRS complex is comprised of three phases: 1. phase to the right and downward, 2. phase to the left and downward, 3. phase in the upward direction.

c*. Analysis of the effective dipole depth.

Normal parameter during the ST-T interval - the depth at the J point should be primarily within the interval.

Normal parameter during the QRS complex - four different movements of a dipole in the depth are in existence. The first movement is oriented forwardly, the second movement (the main one) is directed to the rear, the third movement is forwardly oriented, the fourth movement is directed to the rear.

D. Visual estimation of the direction of the current expansion based on the maps of the current lines and the maps of the current density vectors.

E*. Quantitative analysis of the expansion direction of the current based on the maps of the current lines and the maps of the current density vectors.

Normal orientation during the ST-T interval is to the left and downward (during not more than 2/3 of the duration of the ST-T interval).

Normal direction during the QRS complex is comprised of three phases: 1. phase to the right and downward, 2. phase to the left and downward, 3. phase in the upward direction.

The main clinical significance of this group of criteria is the determination of

heart disturbances in general, in particular, the diagnosis of different forms of ischemia and the estimation of the efficiency of an anti-ischemic therapy.

Group 4. Criteria for the analysis of absolute and relative intensity of the electrical process in the myocardium.

A*. Analysis of the relative atria to the ventricular electrical activity (P/QRS integral ratio). The normal value - not more than 0.13).

B*. Analysis of the current density value.

Normal values are:

- the ratio of current density at the point in time 80 msec after ST onset relative to the current density at the J point should not be smaller than 2.5.
- the ratio of the current density values at the R-max point to the T-max point should not be greater than 3.5.

The main clinical significance of this criteria group is the determination of heart disturbances in general, in particular, the diagnosis of different forms of ischemia and heart failure, as well as the estimation of therapy efficiency.

The large number and structure of criteria reflects the many aspects of the information contained in the MCG and also the historic direction of software development: from the morphological analysis of the MCG curves to solving the two-dimensional inverse problem.

At present, in the practical work all above-mentioned sets are used. Sometimes, inconsistencies between these criteria (for example, one indicator corresponds to the standard, while another one shows an abnormal value) exist in the analysis of the MCG of some patients . This is the reason why it is necessary, based on discriminating cluster analysis or other mathematical methods for the pattern recognition, to carefully determine the informative possibilities of each indicators and subsequently to set forth a set of formalized solving rules for different clinical objectives which can operate automatically. Then it is possible to reject certain criteria.

Diagnostic criteria for the diagnosis of myocardial ischemia by employing magnetocardiographic data.

Quantitative analysis of the maps of distribution of the ventricular magnetic repolarization field

- According to the right-hand rule the approximate direction of the corresponding current dipoles in each map is determined and their deviation from the normal direction to the left and downward is determined.
- The presence of additional extreme values in each magnetic field distribution map is determined.
- Quantitative analysis of the ventricular magnetic repolarization field distribution map.
- The ordinal number of the map is determined based on that one in which the direction of the equivalent ventricular repolarization current dipole become stably normal, i.e., pointed to the left and downward (during not more than 1/3 of the ST-T interval duration, wherein the greater the ordinal number of the mentioned map, the greater the severity of ischemia).
- Duration of existence of additional extreme values during the repolarization process is estimated (not more than 1/3 of the duration of the ST-T interval, the greater the duration of the existence of additional extreme values, the greater the severity of ischemia).

Analysis of the effective dipole parameters within the ST-T interval

- The effective dipole depth at the J point is estimated (the depth at this point should be the greatest within the ST-T interval).

Quantitative analysis of the ventricular repolarization tension lines and density vector maps.

- The approximate direction of the most current density vectors in each map is estimated and its deviation from the normal direction to the left and downward is determined.

- The presence of additional current vortices in each current line map is determined.

Quantitative analysis of the ventricular repolarization tension lines and density vector maps.

- The ordinal number of the map is determined, based on the map in which the direction of the most current density vectors became stably normal, i.e., oriented to the left and downward (not more than 1/3 of the duration of the ST-T interval, the greater the ordinal map number, the greater the severity of ischemia).
- The duration of the existence of additional vortices is determined (not more than 1/3 of the duration of the ST-T interval, the greater the duration of the existence of the additional vortices, the greater the severity of ischemia).

Quantitative current density parameters within the ST-T interval

- The ratio of the current density at the point in time 80 msec after ST onset to the current density at the J point is determined (it should not be smaller than 2.5).
- The ratio of the current density values at the R max point to the T max point is calculated (it should not be greater than 3.5).

Any following step of analysis supplements the information of the preceding step and expands on it.

On the basis of all of the above-mentioned criteria the conclusion in regard to the presence and severity of myocardial ischemia is drawn.

The following further advantageous developments are suggested. Two of them are the principal ones and disclose an "instrument set" for the comprehensive analysis of the ventricular repolarization or depolarization. Two further patents are dedicated to the differentiation of the most important heart diseases: chronic ischemia and myocardial infarct. In the future it will be possible to provide the diagnostic methods for some other heart diseases.

1) Method for evaluating the ventricular repolarization using magnetocardiographic data.

3) The problem is the following: the determination of the electro-physical properties of the ventricular repolarization, which has the utmost significance, by using magnetocardiography, wherein the properties can serve as a criterion for the separation of normal and pathological functional states of the heart and for formulating conclusions in regard to certain heart diseases.

The suggested method is based on different sequential steps of the MCG analysis: visual qualitative and quantitative analysis of the magnetic field distribution maps, analysis of the effective current dipole localization, qualitative and quantitative criteria of the current distribution. All these steps make it possible to carry out a comprehensive, accurate, and versatile estimation of the homogeneity of the excitation, the direction of the currents, the efficiency characteristic of the excitation at any point in time and the behavior of all these parameters during the entire repolarization process. In addition to these criteria, the analysis of the effective dipole depth makes possible not only to obtain two-dimensional distributions of the source, but, to a certain degree, also its three-dimensional distribution.

Important new innovations of the presented invention are:

a) sequential applications of different steps of the MCG analysis.

b) estimation of the directional changes of the equivalent current dipole on the magnetic field distribution maps and on the maps of the current line distribution during repolarization.

c) estimation of the effective dipole depth curve.

d) criteria (curves of maximum and average density of a current during repolarization) based on an estimation of the efficiency characteristics.

All of the above-mentioned criteria make it possible to estimate the ventricular repolarization process more comprehensively, more detailed, and more precisely and to draw conclusions based on this in regard to the functional state of the myocardium.

Method for evaluation the ventricular depolarization by using magnetocardiographic data.

The program is the following: determination of the most significant electrophysical properties of the ventricular depolarization by using magnetocardiography which can serve as criteria for the differentiation of normal and pathological functional states of the heart and also for obtaining information in regard to different heart diseases.

There are different methods for evaluation of the ventricular depolarization, i.e.: method of late fields, method of visual estimation of momentary magnetic field distribution maps and temporally integrated maps, method of qualitative and quantitative evaluation of residue maps, method of evaluation of effective current dipole parameters, method of current density calculation.

The first of these methods represents the spectral analysis of the last part of the QRS complex, comparable to the analysis of the late potentials of the ECG. The second method is the analysis of the alternating arrangement of positive and negative extreme values in each magnetic field distribution map. The third method is a visual and quantitative estimation of the differences between the actual map and the reconstructed normal map. The fourth method is the estimation of the orientation and strength of the current dipoles during the QR interval. The fifth method is an estimation of the current density distribution and the values in the QRS maximum vectors at the different points in time of depolarization.

Each of these known methods makes possible the estimation of only one aspect of ventricular depolarization: homogeneity of the excitation or direction of the equivalent current dipoles or current density at defined points in time of the depolarization. Therefore, there are no quantitative criteria which make it possible to estimate the depolarization process not only at discrete points in time but during the entire process. Any of these methods is based only on one step of the analysis: on the magnetic field distribution maps or the parameters of effective dipoles or the

current density distribution maps.

The suggested method is based on different sequential steps of the MCG analysis: visual qualitative and quantitative analysis of the magnetic field distribution maps, analysis of localization of effective current dipoles, qualitative and quantitative criteria of the current distribution. All of these steps make it possible to provide a comprehensive, precise, and versatile estimation of the homogeneity of the excitation, the direction of the currents, the efficiency characteristic of the excitation at any point in time, and the behavior of all these parameters during the entire depolarization process. In addition, the criteria based on the analysis of the effective dipole depth enable not only obtaining the two-dimensional distribution of a source but, to a certain degree, also its three-dimensional distribution.

Important new innovations of the presented invention are:

a) consecutive application of different steps of the MCG analysis.

b) estimation of the directional changes of the equivalent current dipoles on magnetic field distribution maps and on maps of current line distribution during the depolarization.

c) estimation of the effective dipole depth curves.

d) criteria which are based on the efficiency characteristic estimation (curves of maximum and average density of a current during the depolarization) during the entire depolarization process.

All of the above mentioned criteria make it possible to estimate the ventricular depolarization process more comprehensively, more detailed, and more precisely and to draw conclusions in regard to the functional myocardial state based thereon.

Method for diagnosis of myocardial ischemia by employing magnetocardiographic data for patients with unchanged ECG at rest.

The problem is the following: MCG determination of electro-physical properties of the ventricular repolarization which is the result of myocardial

ischemia. This is of special importance in patients with non-informative ECG.

There are two methods for MCG ischemia diagnosis in patients with unchanged ECG, i.e.: method of visual estimation of magnetic field distribution maps and evaluation methods of the effective current dipole parameters. The first of these methods is a visual estimation of the quantity and arrangement of magnetic extreme values and the direction of the dipoles in different moments during the repolarization.

The second method is an estimation of the direction and the strength of the current dipoles in defining moments of the cardial cycle.

A disadvantage of the first of these methods is the fact that only the spatial distribution of the magnetic fields can be obtained without consideration of the direction of the dipoles and the efficiency characteristic. Conversely, the second method does not take into consideration the spatial distribution of the magnetic field. A common disadvantage of both methods is the lack of quantitative criteria which make it possible to estimate the repolarization process not only at a discrete point in time but during the entire process. These methods are not able to estimate the severity of the ischemia. Each one of them enables only the estimation of one aspect of the ventricular repolarization: the homogeneity of the excitation or the direction of the equivalent current dipoles and the strength at certain moments of repolarization.

The suggested method is based on different sequential steps of the MCG analysis: visual qualitative and quantitative analysis of the magnetic field distribution maps, analysis of localization of the effective current dipoles, qualitative and quantitative criteria of the current distribution. All of these steps make possible a comprehensive, precise and versatile estimation of the excitation homogeneity, the direction of the currents, the efficiency characteristic of the excitation at any point in time, and the behavior of all these parameters during the entire repolarization process. In addition, the criteria based on the analysis of the effective dipole depth

make it possible to obtain not only two-dimensional distributions of a source but, to a certain degree, also their three-dimensional distribution. This makes it possible to improve the sensitivity and specificity of a method significantly and to diagnose not only the presence of ischemia but also to estimate its degree.

Important new innovations of the proposed invention are:

a) sequential application of different steps of the MCG analysis

b) estimation of the directional changes of the equivalent current dipoles on magnetic field distribution maps and on maps of distribution of current lines during repolarization

c) evaluation of additional extreme values and the current area lifetime during the repolarization

d) estimation of the effective dipole depth curve

e) criteria based on an estimation of the efficiency characteristics (curves of maximum and average density of current during repolarization).

All of the above-mentioned criteria make it possible to significantly improve the sensitivity and precision of the diagnosis of myocardial ischemia by means of MCG in patients with unchanged the ECG.

Method for diagnosis of myocardial necrosis by using magnetocardiographic data.

The problem is the following: determination of the myocardial necrosis which is the result of a myocardial infarct, i.e., development of MCG equivalents of the myocardial necrosis.

There are different methods of evaluation of myocardial necrosis by using MCG, i.e.: method of morphological analysis of the QRS complex, method of visual estimation of delay-free magnetic field distribution maps and temporally integrated maps, method of qualitative and quantitative evaluation of residue maps, evaluation method of the effective current dipole parameters, method of calculation of current densities.

The first method represents the estimation of the QRS complex type in different measured points, equivalent to standard ECG analysis.

The second method represents the analysis of the alternating arrangement of positive and negative extreme values in each magnetic field distribution map. The third method represents a visual and quantitative estimation of the differences between the actual map and a reconstructed normal map. The fourth method represents an estimation of the direction and strength of the current dipole during the QRS interval. The fifth method represents an estimation of the current distribution and the values in the QRS maximum vectors at different points in time of the depolarization.

Each of these methods makes it possible to estimate only one aspect of the ventricular depolarization: homogeneity of the excitation or direction of the equivalent current dipole or current density at defined points in time of depolarization. Accordingly, there are no quantitative criteria which make it possible to estimate the depolarization process not only at certain points in time but during the entire process. Each of these methods is based only on one step of the analysis: on magnetic field distribution maps or defective dipole parameters or current density distribution maps. Only the second method is used for diagnosis of non-Q-infarcts, that is, in patients with non-informative or inconclusive ECG.

The proposed method is based on different sequential steps of MCG analysis: visual qualitative and quantitative analysis of magnetic field distribution maps, analysis of localization of effective current dipoles, qualitative and quantitative criteria for the current distribution. All of these steps make possible a comprehensive, precise, and versatile estimation of the homogeneity of excitation, the direction of the currents, the efficiency characteristic of the excitation at any point in time, the behavior of all these parameters during the entire depolarization process. In addition, the criteria based on the analysis of the effective dipole depth not only enable the determination of the two-dimensional distribution of the source

but, to a certain degree, also its three-dimensional distribution.

The important new innovations of the proposed invention are:

a) sequential application of different steps of the MCG analysis.

b) estimation of the directional changes of the equipment current dipoles on magnetic field distribution maps and on maps of current line distribution during the depolarization.

c) estimation of the effective dipole depth curves.

d) criteria based on the estimation of efficiency characteristics (curves of the maximum and average density of a current during depolarization) during the entire depolarization process.

All of the above-mentioned criteria make it possible to significantly improve the sensitivity and precision of diagnoses of myocardial necrosis by means of MCG.

In Fig. 1 the most important steps for performing the method according to claim 1 are illustrated in the form of a flowchart.

For calculating the sources of a measured biomagnetic field two parallel, for example, square surfaces are considered which have a spacing h from one another. The "upper" surface S_m is referred to as measuring plane, the "lower" surface S_s is referred to as source plane. The magnetic field is measured by gradiometers of the second order which are positioned above the measuring plane such that the recording coil (pickup coil) is positioned in the measuring plane. The measurement of a signal is carried out within the overlapping centers of a pickup coil with n x n nodes in this plane. The grid of m x m nodes is selected on S_s.

The integral equation (IE) Ax=y is solved wherein the coefficients of a matrix a_{ij}, i=1, n^2, j=1, m^2 are defined by the expression $s=s_1-2s_2+s_3$. The components of $s_1-2s_2+s_3$ are vertical (z) components of the magnetic induction at the points Q_i, Q'_i, Q''_i, wherein Q_i is a node of a grid and the points Q'_i, Q''_i are above S_m within the two distances b and 2b wherein b is the baseline of the gradiometer. The coefficient a_{ij} depends also on the position of a node Mj on a grid S_s. The right part of the

equation represents the distribution in the nodes Q_i of a signal of a gradiometer.

After solving IE by means of SV decomposition of a current function or a distribution of the magnetic moments, one obtains ô in a source plane. Its iso-lines are current lines. The distribution of the current density vectors can be found by means of the equation j=[grad x, n].

For the definition of the distances between the plane S_s and S_m - i.e., the "depth" - the following procedure is used: the problem for the values h_k, k=1,p is solved and a position on the plane S_s is determined for which the standard $||x_{k^*}||/(x_i)_{max}$ is minimal. The determined value h_{k^*} is improved by guiding a parabola through the points h_{k^*-1}, h_{k^*}, h_{k^*+} and determining a position of a minimum of this parabola.

Step of Examination	Examined Physical Substrate	Informative Criteria	Appearance of Resulting Information
visual qualitative examination of MCG at each of 36 recording points	magnetic field relative to time dependence during the cardial cycle at each of 36 recording points	signal/noise ratio	conclusions with respect to suitability of MCG for further examinations
examination of integral MCG	average magnetic field relative to time curve during cardial cycle for different recording points	ratio of integrals P/QRS	conclusions with regard to relative electrical atria in relation to ventricular activity
visual (qualitative) examination of the magnetic field distribution maps	direct and spatial maps of the distribution of magnetic field intensity	occurrence of additional locations of positive and negative values and their reciprocal position	conclusion with regard to normal or reduced homogeneity of the electro-physiological process, provisional observance in the direction of EMF (electromagnetic force)
quantitative analysis of magnetic field distribution maps	direct spatial maps of distribution of magnetic field intensity and its variations during the cardial cycle	number of extreme values, IH, KH, ∂ min/max, map number with normal orientation of EMF (electromagnetic field strength vector)	conclusions with regard to homogeneity rate of atria and ventricular excitation and abnormalities of EMF orientation during ventricular repolarization
analysis of effective points of the dipole path	variations of the effective dipole position during the cardial cycle	type of effective dipole depth curve during the cardial cycle, visual criteria of effective dipole position variability ∂z during the ventricular repolarization	orientation of inhomogeneity and other electro-physiological disturbance rates and types, including distribution of sources in the sagittal plane
qualitative and quantitative analysis of two-dimensional charge distribution	direct spatial maps of current lines and the distribution of current density vectors	visual and quantitative criteria which make it possible to estimate the number of sources, their location, relative intensity, the direction of flowing current, and the variation of these parameters during the cardial cycle, curves of maximum and average current density	further orientation of inhomogeneity and other electro-physiological disturbance rates and types, estimation of the relative intensity of normal and the pathological sources and approximate localization of the failing zones of the myocardium, estimation of energetic excitation parameters (current density)

integrated conclusions with respect to inhomogeneity rate and the type of myocardiological electro-physiological process, directions of momentary electromagnetic force (EMF) and the current density, electrical atria and ventricular activity.

conclusions with respect to different forms of myocardial ischemia, superventricular and ventricular arrhythmia risks, rate of heart failure, changes of the electro-physiological process under treatment or diagnostic tests.

Table 1

Claims

1. A computer-based method for automatically processing data of biomagnetic fields, in particular, of magnetocardiographic data, comprising the following steps based on a surface density of magnetic moments (layer of magnetic dipoles) or, which is equivalent thereto, a function of currents as physical and mathematical models of the sources of the biomagnetic field:

- stating an integral equation concerning the surface density of the magnetic moments whose right term represents the second differentiation of the magnetic field induction measured by a gradiometer in the normal direction to the measuring plane ($\partial^2 B_z/\partial z^2$);
- determining analytical expressions for factors of a matrix A which approximates the integral operator of the aforementioned integral equation and computing this matrix;
- interpolating the measured values of the function $y=\partial^2 B_z/\partial z^2$ in the nodes of a preferably small-dimensioned grid;
- solving according to Tickhonov a linear algebraic equation system $Ax=y$, wherein x is the surface density of the magnetic moments;
- constructing contour line maps of the surface density of the magnetic moments or, which is equivalent thereto, a current line map and reading the map into a storage unit or an output unit.

2. A method according to claim 1, characterized in that the gradient of the surface density of the magnetic moments is automatically calculated and the map of the current density is constructed and is read into a storage unit or an output unit.

3. A computer-based method for automatically processing data of

biomagnetic fields, in particular, of magnetocardiographic data, in particular, according to claim 1, characterized in that at least selected data are compared according to predetermined criteria automatically with at least one predefined normal value and that, upon deviation of the data from the normal value by a predetermined amount, a signal is generated which can be output on an output device and which signals the deviation.

4. A method according to claim 3, characterized in that the magnitude of the fields under the P-wave and the QRS complex are calculated. The magnitude of these fields reflects the energy which is generated during the excitation of the atria and ventricles of the heart. Moreover, the ratio of these fields can be calculated in order to estimate in this way the electrical activity of the atria in comparison to the electrical activity of the ventricles. It was found that these parameter is related to the degree of heart failure.

5. A method according to one of the claims 1 to 4, characterized in that one of the parameters described in the specification is automatically calculated based on the measured data and compared with a normal value.

6. A method according to one of the claims 1 to 5, characterized in that the measured data automatically pass through different analysis steps, wherein the complexity of the analysis increases with each step.

7. A method according to claim 6, characterized in that at least one of the following analysis steps are employed: amplitude-time analysis of different MCG curves; analysis of high-resolution MCG; analysis of the sum of MCG and vector MCG (VMCG); qualitative analysis of the magnetic field distribution maps; quantitative analysis of the magnetic field distribution maps; analysis of the

effective dipole characteristics; analysis of two-dimensional charge distribution; analysis of three-dimensional charge distribution.

8. A computer-based method for automatically processing magnetocardiographic data, comprising the steps of:

- estimating the alternating arrangement of maximum positive and negative extreme values in each magnetic field distribution map;
- estimating the direction of equivalent current dipoles in each map by using the right-hand rule;
- estimating the presence of additional extreme values in each magnetic field distribution map and duration of their existence during the repolarization process;
- calculating the ratio of the maximum negative to the maximum positive extremes in each map and of the standard differentiation of these parameters during the method;
- estimating the effective dipole depth curve in the repolarization;
- estimating the distribution and alternating arrangement of current line and the directions of current line vectors in each map during the repolarization;
- estimating the curves of average and maximum current density during repolarization;
- automatic evaluation of ventricular repolarization with respect to conformity of the actual repolarization process in comparison to normal parameters.

9. A computer-based method for automatically processing magnetocardiographic data, comprising the following steps:

- estimating the alternating arrangement of maximum positive and negative extreme values in each magnetic field distribution map;

- according to the right-hand rule estimating the direction of the equivalent current dipole in each map;
- estimating the presence of additional extreme values in each magnetic field distribution map and the duration of their presence during the depolarization process;
- estimating the effective dipole depth curve during the depolarization;
- estimating the distribution and alternating arrangement of current lines and the directions of the current density vectors in each map during the depolarization;
- estimating the duration of existence of additional current areas during the depolarization process;
- estimating the curve of average and maximum current density during the depolarization;
- automatic evaluation of conformity of the actual the depolarization process with normal parameters.

10. A computer-based method for automatically processing magnetocardiographic data, comprising the following steps:
- estimating the alternating arrangement of maximum positive and negative extreme values in each magnetic field distribution map;
- estimating according to the right-hand rule the direction of equivalent current dipoles in each map;
- estimating the presence of additional extreme values in each magnetic field distribution map and the duration of their existence during the repolarization process;
- the ordinal number of the map beginning at the point in time at which the direction of the equivalent current dipole of the ventricular repolarization became stably normal, i.e., to the left and downward;

- estimating the effective dipole depth at the J point;
- estimating the distribution and alternating arrangement of the current lines and the directions of current density vectors in each map during the repolarization;
- determining the ordinal number of the map beginning at the point in time at which the direction of maximum current density vector of the ventricular repolarization became stably normal, i.e., oriented to the left and downward;
- estimating the duration of existence of additional current areas during repolarization process;
- estimating the curves of average and maximum current density during the repolarization at the beginning of the ST-T interval;
- estimating the ratios of maximum and average current densities in the QRS maximum relative to those at T-maximum;

Automatically evaluating the estimations with respect to the presence and severity of myocardial ischemia, in particular, in patients with unchanged ECG at rest comprising the following steps:

11. A computer-based method for automatically processing magnetocardiographic data, comprising the following steps:
- estimating the alternating arrangement of maximum positive and negative extreme values in each magnetic field distribution map;
- estimating according to the right-hand rule the direction of the equivalent current dipoles in each map;
- determining the time periods during which the direction of the effective dipoles remains oriented 1. to the right or to the right and downward, 2. to the left and downward, 3. to the right or or upward;
- estimating the presence of additional extreme values in each magnetic field distribution map and the duration of their existence during the depolarization

process;

- estimating the relative amplitude of the upwardly and downwardly oriented movement of the effective dipoles during the depolarization;
- estimating the distribution and alternating arrangement of a current line and the directions of current density vectors in each map during the depolarization;
- determining the time period during which the direction of maximum current density vectors remains oriented 1. to the right or to the right and downward, 2. to the left and downward, thirdly, to the right or to the right and upward;
- estimating the duration of existence of additional current areas during the depolarization process;
- estimating the peak values of the average and maximum current density during the depolarization and the form of the corresponding curves;

automatic evaluation of the estimations with respect to the presence of myocardial necrosis.

12. A computer-based method for automatically processing data of biomagnetic fields, in particular, of magnetocardiographic data, as disclosed in the specification.

13. A method according to one of the claims 1 to 12, characterized in that upon comparison of the considered data with normal values, the considered data are automatically stored in a self-learning database and, according to predetermined criteria, can be employed for a continuous formation and checking of normal values and tolerable deviations of the normal values.

14. Use of one of the claimed and/or described methods for automatic analysis of data of a patient, preferably of the data of greater numbers of

patients in the context, in particular, of a screening test, for evaluating the risks of certain diseases, in particular, one of the heart diseases mentioned in the application.

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(71) Anmelder *(für alle Bestimmungsstaaten mit Ausnahme von US)*: **SQUID AG** [DE/DE]; Kruppstrasse 94, 45145 Essen (DE).

(71) Anmelder *(nur für US)*: **ROMANOVYCH, Stella** (Erbin des verstorbenen Erfinders) [UA/DE]; c/o Squid AG, Kruppstrasse 94, 45145 Essen (DE).

(72) Erfinder: **ROMANOVYCH, Stepanowitsch** (verstorben).

(72) Erfinder; und
(75) Erfinder/Anmelder *(nur für US)*: **STEINBERG, Fritz** [DE/DE]; Mausegattstrasse 29, 45472 Mülheim an der Ruhr (DE).

(74) Anwalt: **KREUTZER, Ulrich**; Kruppstrasse 92, 45145 Essen (DE).

(81) Bestimmungsstaaten *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,

[Fortsetzung auf der nächsten Seite]

(54) Title: COMPUTER-BASED METHOD FOR AUTOMATICALLY PROCESSING DATA, ESPECIALLY MAGNETOCARDIOGRAPHIC DATA, OF BIOMAGNETIC FIELDS

(54) Bezeichnung: COMPUTERBASIERTES VERFAHREN ZUR AUTOMATISCHEN AUFBEREITUNG VON DATEN BIOMAGNETISCHER FELDER, INSBESONDERE VON MAGNETOKARDIOGRAPHISCHEN DATEN

(57) Abstract: The aim of the invention is to provide a method for processing data of the detected biomagnetic field. Fluxes which cause the biomagnetic field can be visualised in the level by means of flux lines and the inventive method in such a way that trained personnel or a doctor has access to said fluxes in a particularly simple manner for the visual evaluation thereof. Disclosed is a computer-based method which comprises the following steps that are based on a surface density of magnetic moments (layer of magnetic dipoles) or a function of the fluxes, whereby said function is equivalent to said surface density. The surface density or the function represents a physical and mathematical model of the sources pertaining to a biomagnetic field. Said steps are: An integral equation relating to the surface density of magnetic moments is constructed. The right term of said equation represents the second differentiation of the magnetic field induction in the normal direction to the measuring level ($\partial^2 B_z/\partial z^2$). Said differentiation is measured by a gradiometer. Analytical expressions for factors of a matrix A which approaches the integral operator to said integral equation are determined. The matrix is calculated. The measured values of the function $y=\partial^2 B_z/\partial z^2$ are interpoled into the node of a grid having, preferably small, dimensions. A linear algebraic equation system $Ax = y$ is solved according to Tickhonov, whereby x is the surface density of the magnetic moments. A contour line card of the surface density pertaining to the magnetic moments or a flux line card being equivalent thereto is established. The card is read out into a storage unit or an output unit.

(57) Zusammenfassung: Der Erfindung liegt die Aufgabe zugrunde, ein Verfahren zum Aufbereiten der Daten des erfaßten biomagnetischen Feldes anzugeben, mittels welchem die das biomagnetische Feld hervorrufenden Ströme durch Stromlinien in der Ebene derart visualisiert werden können, daß sie einer visuellen Auswerfung durch geschultes Personal oder einen Arzt in besonders einfacher Weise zugänglich werden. Es wird ein computerbasiertes Verfahren vorgeschlagen, das die folgenden, auf einer Oberflächendichte magnetischer Momente (Schicht magnetischer Dipole) oder, was äquivalent hierzu ist, einer Funktion der Ströme als physikalisches und mathematisches Modell der Quellen eines biomagnetischen Feldes beruhenden Schritte umfaßt: Aufstellen einer die Oberflächendichte der magnetischen Momente betreffenden Integralgleichung, deren rechtes Glied die von einem Gradiometer gemessene zweite Ableitung der magnetischen Feldinduktion in Normalenrichtung zur Meßebene ($\partial^2 B_z/\partial z^2$) darstellt; Bestimmen analytischer Ausdrücke für Faktoren einer Matrix A, die den integralen Operator der genannten Integralgleichung annähert, und Berechnung dieser Matrix; Interpolation der gemessenen Werte der Funktion $y=\partial^2 B_z/\partial z^2$ in den Knoten eines vorzugsweise klein dimensionierten Gitters; Lösung gemäß Tickhonov eines linearen algebraischen Gleichungssystems $Ax=y$, wobei x die Oberflächendichte der magnetischen Momente ist; Aufbau einer Niveaulinienkarte der Oberflächendichte der magnetischen Momente oder, was äquivalent hierzu ist, einer Stromlinienkarte und Auslesen der Karte in eine Speichereinheit oder eine Ausgabeeinheit.

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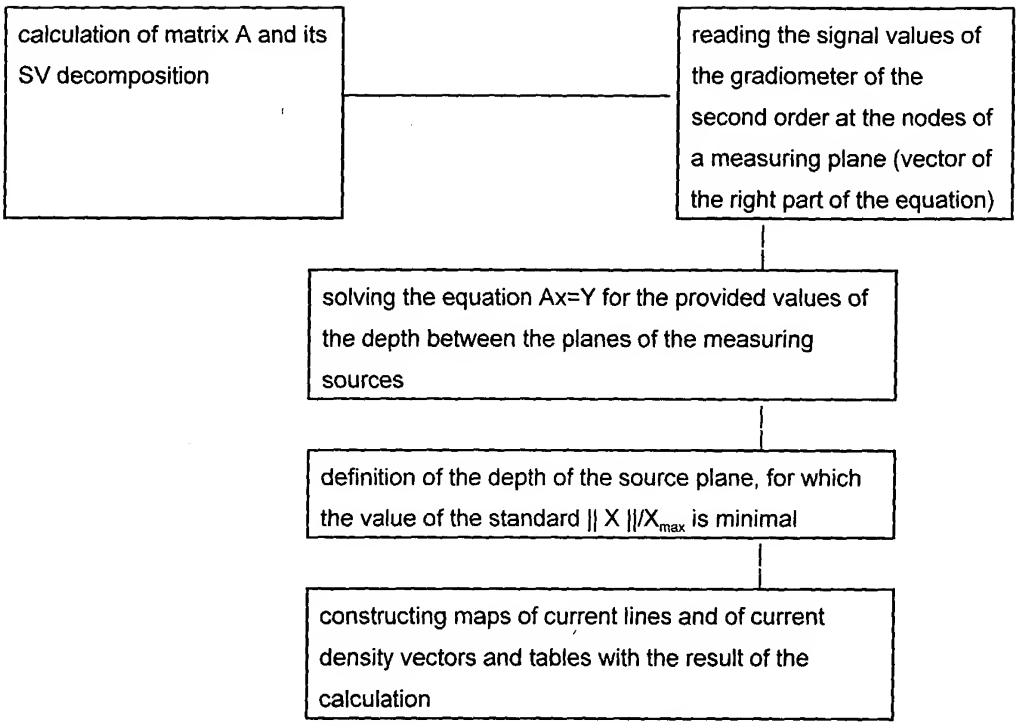
calculation of matrix A and its SV decomposition
reading the signal values of the gradiometer of the second order at the nodes of a measuring plane (vector of the right part of the equation)
solving the equation Ax=Y for the provided values of the depth between the planes of the measuring sources
definition of the depth of the source plane, for which the value of the standard || X ||/X_{max} is minimal
constructing maps of current lines and of current density vectors and tables with the result of the calculation

Fig. 1

Attorney Docket No. S04P03US

DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63)

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought of the invention entitled:

Computer-Based Method for Automatically Processing Data, Especially Magnetocardiographic Data, of Biomagnetic Fields

the specification of which
[ ] is attached hereto; or
[X] was filed on **2/28/2002**
as US Application Ser. No. **10/070,347**
or PCT Application No.
and was amended on _____.

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56.

I hereby claim foreign priority benefits under Title 35 U.S.C. 119 (a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or 365(b) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or any PCT international application having a filing date before that of the application on which priority is claimed:

Prior Foreign Application Ser. No.	Country	Foreign Filing Date (Month/Day/Year)	Priority Claimed	
			Yes	No
19940912.9	Germany	8/28/1999	X	

Attorney Docket No. S04P03US

I hereby claim the benefit under 35 U.S.C. § 119(e) of any United States provisional application(s) listed below:

Application No.	Filing Date (Month/Day/Year)

I hereby claim the benefit under Title 35 U.S.C. 120 of any United States application(s), or 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of 35 U.S.C. 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

U.S. Parent Application or PCT Parent No.	Parent Filing Date (Month/Day/Year)	Parent Patent No.

As a named inventor, I hereby appoint the following registered practitioner to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

GUDRUN E. HUCKETT, REGISTRATION NO. 35,747

Direct all correspondence and communications to the correspondence address and telephone and fax numbers below:

GUDRUN E. HUCKETT, PATENT AGENT
Lönsstr. 53
42289 Wuppertal
GERMANY
Telephone: +49 (202) 257-0371
Fax: +49 (202) 257-0372
E-mail: gudrun.huckett@t-online.de

Attorney Docket No. S04P03US

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

1-01

Full name of sole or first inventor: **Stepanowitsch Romanovych** (deceased)
Last Residence: Timoschenko St. 2a, Apartment 38, Kiev 212, Ukraine
Citizenship: Ukraine
Post Office Address: same as above

2-11

Signed by **Stella Iwanowa,** heiress and legal representative

Signature: _____ Date: 05. Feb. 2003
Residence: Timoschenko St. 2a, Apartment 38, Kiev 212, Ukraine UAX
Citizenship: Ukraine
Post Office Address: same as above

3-00

Full name of second inventor, if any: **Fritz Steinberg**

Inventor's signature: _____ Date: 05. Feb. 2003
Residence: Mausegattstr. 29, 45472 Mülheim an der Ruhr, Germany DEX
Citizenship: German
Post Office Address: same as above